REMARKS

Claims 1-52 were pending in the instant application. In a Response to Restriction Requirement earlier filed on November 29, 2005, Applicants elected with traverse to pursue prosecution of Group I, claims 1-6. Applicants hereby affirm the election with traverse of Group I, claims 1-6 and 52. Upon entry of the present Amendment, claims 1-52 are pending and presented for reconsideration. Applicants respectfully submit that no new matter is introduced by the present Amendment.

Amendment and/or cancellation of the claims is not to be construed as acquiescence to any of the objections/rejections set forth in the instant Office Action or any previous Office Action of the parent application, and was done solely to expedite prosecution of the application. Applicants submit that claims were not added or amended during the prosecution of the instant application for reasons related to patentability. Applicants reserve the right to pursue the claims, as originally filed, or similar claims in this or one or more subsequent patent applications.

Rejection of Claims 1-6 and 52 under 35 U.S.C. §112, First Paragraph

Claims 1-6 and 52 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Office Action, on page 5, states that "[t]he specification as currently presented while describing the treatment of a microbial infection via administering a modulator of a transcription factor to an individual in need thereof does not provide support for a method to prevent said infecting in an individual." Applicants traverse the foregoing rejection on the grounds that one of ordinary skill in the art would understand that Applicants were in possession of the claimed invention.

The pending claims are directed to a method for an preventing infection, *e.g.*, prostatitis or urinary tract infection, of a subject by a microbe comprising: administering a compound that modulates the expression or activity of a microbial transcription factor to a subject at risk of developing an infection, wherein the modulation of the microbial transcription factor reduces the virulence of the microbe, such that infection is prevented. For the reasons set forth below, Applicants respectfully submit that the claimed invention is supported by the specification on record and that the instant specification conveys to the ordinary skilled artisan that the inventor(s) had possession of the claimed invention at the time the application was filed.

An objective standard for determining compliance with the written description requirement under 35 U.S.C. § 112, first paragraph, is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, the applicant was in possession of the invention as now claimed. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991) and In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

To begin with, the Examiner has admitted, at page 5 of the Office Action, that the specification describes "***the treatment of a microbial infection via administering a modulator of a transcription factor to an individual in need thereof***."

Moreover, Applicants respectfully submit that Applicants' specification provides extensive teachings on methods for preventing infection of a subject by a microbe comprising: administering a compound that modulates the expression or activity of a microbial transcription factor to a subject at risk of developing an infection, wherein the modulation of the microbial transcription factor reduces the virulence of the microbe, such that infection is prevented. Firstly, Applicants respectfully submit that the specification provides a plethora of teachings which would enable one of ordinary skill in the art to generate and assay the claimed compounds for functional activity. For example, the specification teaches at least at page 38, line 1 through page 50, line 3, a multitude of whole cell assays that can be performed in order to determine whether a compound reduces the activity or expression of a transcription factor by contacting a cell expressing a transcription factor with a compound and measuring the ability of the compound to modulate the activity and/or expression of a transcription factor. Specifically, Applicants teach at least at page 38, lines 26-29, that "transcription of a transcription factor gene can be measured in control cells which have not been treated with the compound and compared with that of test cells which have been treated with the compound..." and that transcription can be determined by measuring the amount of RNA produced by the cell (see, *e.g.*, page 39, lines 19-31), by measuring the amount of transcription factor produced by a cell (see, *e.g.*, page 39, line 32 through page 40, line 6), by detecting other sequences which are regulated by a transcription factor, *e.g.*, using a reporter gene (see, *e.g.*, page 40, line 7 through page 41, line 30), by measuring the binding of a transcription factor to a transcription factor binding molecule (see, *e.g.*, page 41, lines 31 through page 42, line 2), etc. Additionally, Applicants' specification teaches at least at page 50, line 8 through page 58, line 2, cell-free assays for screening for

inhibitors of transcription factors. Furthermore, Figure 3 exemplifies cell-free assays of Mar inhibitors.

Not only do Applicants teach methods for the generation and testing of the claimed compounds for activity *in vitro*, but Applicants also teach *in vivo* models of suitable for testing the ability of the claimed compounds to prevent infection of a subject. Applicants' specification explicitly teaches at least at pages 126-127, Example 7, two inhibitors of transcription factors that were tested in a working example, the urinary tract infection model. In this experiment, Applicants teach that "mice were treated once, at the time of infection," and ***treatment with a dose of 100 mg/kg of inhibitor prevented infection in 100% of the mice tested***, *e.g.*, 0 out of 5 mice were infected (see, *e.g.*, the chart on page 127 of the specification). Furthermore, Applicants further teach that lower doses of inhibitor, *e.g.*, 10 mg/kg and 1 mg/kg, can also prevent infection in a substantial percentage of the mice (see, *e.g.*, the chart on page 127 of the specification).

The specification also provides extensive teachings on how to prevent infection using inhibitors of transcription factors in animal models, *e.g.*, in the pyelonephritis model of infection. At, for example, page 132, lines 28-31 of the specification, Applicants teach that "***the administration of a single subcutaneous dose of the inhibitor at the time of infection was sufficient to prevent infection in this [pyelonephritis] in vivo model.***" Figure 10 exemplifies these results, and similar results were also observed using smaller doses with multiple dose regiments (see, *e.g.*, Figure 10 and page 132, lines 31-33 of the specification).

In addition to the foregoing extensive teachings in Applicants' specification, Applicants provide teachings regarding the composition for administration for a method of prophylaxis. For example, Applicants teach pharmaceutical compositions at least at page 84, line 9, through page 90, line 34. Specifically, Applicants teach several routes of administration and typical ingredients of the composition, based upon the route of administration. The specification also discloses exemplary doses, including milligram or microgram amounts of the small molecule per kilogram of subject, *e.g.*, about 1 microgram per kilogram to about 500 micrograms per kilogram, about 100 micrograms per kilogram to about 5 micrograms per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram (see *e.g.*, page 90, lines 17-21 of the specification). Further, Applicants state that "it is understood that the specific dose level for any particular animal subject will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, gender, and diet of the

subject, the time of administration, the route of administration, the rate of excretion, any drug combination, and the degree of expression and/or activity to be modulated" (see, *e.g.*, page 90, lines 29-34).

Finally, Applicants provide several *in vivo* working examples which exemplify these dosages and compositions (see, *e.g.*, Example 7 and Example 12). In Example 7 Applicants provide teachings regarding the composition for administration for a method of prophylaxis in the urinary tract infection animal model. In one experiment, Applicants teach that "mice were treated once, at the time of infection," and treatment with a dose of 100 mg/kg of inhibitor prevented infection in 100% of the mice tested, *e.g.*, 0 out of 5 mice were infected (see, *e.g.*, the chart on page 127 of the specification). Furthermore, Applicants further teach that lower doses of inhibitor, *e.g.*, 10 mg/kg and 1 mg/kg, can also prevent infection in a substantial percentage of the mice (see, *e.g.*, the chart on page 127 of the specification). In a subsequent experiment (see Example 12 on page 132 of the specification), the efficacy of one prototypic inhibitor was investigated in the ascending pyelonephritis model of infection. The administration of a single subcutaneous dose of the inhibitor at the time of infection was sufficient to prevent infection in this *in vivo* model (see Figure 10 of the specification). Furthermore, the specification teaches at page 132, lines 29-33, that "[r]esults similar to those obtained with the single 100 mg/kg dose (Fig. 10) were observed using smaller doses with multiple dose regimens (bid x4 d, data not shown)."

As evidenced by all of the foregoing, one of ordinary skill in the art would understand that Applicants were in possession of the claimed invention. Applicants, therefore, respectfully request withdrawal of the rejection of claims 1-6 and 52 under 35 U.S.C. §112, first paragraph and favorable reconsideration.

CONCLUSION

In view of the foregoing, entry of the amendments and remarks presented, favorable reconsideration and withdrawal of the rejections, and allowance of this application with the pending claim are respectfully requested. If a telephone conversation with the Applicant's attorney would expedite prosecution of the above-identified application, the Examiner is invited to call the undersigned at (617) 227-7400.

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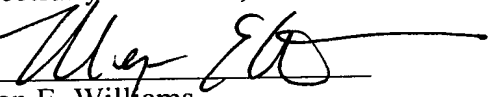
Respectfully submitted,

By 

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